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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/601,273	06/19/2003	Susan J. Braunhut	08688-057001 / UML 02-06	6439

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EXAMINER	
SCHUBERG, LAURA J	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 05/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/601,273	BRAUNHUT ET AL.	
	Examiner	Art Unit	
	Laura Schuberg	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-46* is/are pending in the application.

4a) Of the above claim(s) *21-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20 and 46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/1/03, 05/7/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I (claims 1-20 and 46) in the reply filed on 04/13/2006 is acknowledged.

Claims 21-45 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Information Disclosure Statement

The information disclosure statement filed 12/01/2003 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein for the missing document (Muramatsu et al.) has not been considered.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States

only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-6, 8,9,11,12,16 and19 are rejected under 35 U.S.C. 102(e) as being anticipated by Kanno et al (US 2002/0031827 A1).

Claim 1 is drawn to a method of generating a morphogen composition from an extracellular matrix, the method comprising: growing cells on a surface in a fluid under conditions and for a time sufficient to enable the cells to form an extracellular matrix (ECM); stimulating the extracellular matrix to release morphogens into the fluid; and collecting the fluid to form a morphogen composition.

Claim 2 is drawn to the method of claim 1 wherein the morphogens are growth factors or differentiating factors. (Applicant elected growth factors.)

Claim 3 is drawn to the method of claim 1 wherein the morphogens are differentiating factors, growth factors, bioactive fragments of the ECM, or any combination of two of more of these morphogens. (Applicant elected growth factors.)

Claim 4 is drawn to the method of claim 1 wherein the morphogen composition comprises a plurality of morphogens.

Claim 5 is drawn to the method of claim 1 wherein the fluid comprises a biocompatible liquid or biocompatible gel.

Claim 6 is drawn to the method of claim 1 wherein stimulating the extracellular matrix comprises applying an electric potential to the extracellular matrix.

Claim 8 is drawn to the method of claim 6 wherein the electrical potential ranges from –0.3 V to + 0.3 V.

Claim 9 is drawn to the method of claim 6, further comprising varying frequency, potential range, potential cycle shape, or potential cycle number of the electric potential to control release and activation of specific morphogens.

Claim 11 is drawn to a morphogen composition comprising a plurality of morphogens released from a stimulated extracellular matrix.

Claim 12 is drawn to the composition of claim 11, further comprising a biocompatible fluid.

Claim 16 is drawn to the composition of claim 11, wherein the plurality of morphogens comprises any two or more growth factors, differentiating factors, bioactive fragments of the ECM, or any combination of two or more of these morphogens. (Applicant has elected growth factors.)

Claim 19 is drawn to the composition of claim 11, wherein the extracellular matrix is stimulated by an electric potential.

Kanno teaches a method for electrical stimulation of cells which comprises preincubating cells for 24 hours in DMEM containing 0.1% BSA (p.2 para 25). When the medium is collected for testing of the morphogen (p.3 para 30), the composition collected comprises medium which is a biocompatible fluid. An electric stimulation of 1.0 V is used for some examples, but an electric stimulation of 0.1 V is taught also (claim 2) which is in the same range claimed by Applicant. A morphogen composition is collected and tested for VEGF (vascular endothelial growth factor)(p.2 para 26). While the reference is silent to the presence of other morphogens in the composition, they are inherently present since the reference is carrying out the same method as claimed by

Applicant. The reference also teaches that the frequency and voltage of the electrical current may be varied depending upon need (p.2 para 21). The presence of other growth factors in the morphogen composition is taught as well (p.3 para 32).

Claims 1-7, 11, 12, 16, 17 are rejected under 35 U.S.C. 102(e) as being anticipated by Wolf et al (US 6,485,963 B1).

Claims 1-6 are drawn to the method of claim 1 as described above.

Claims 11,12 and 16 are drawn to the composition as described above.

Claim 7 is drawn to the method of claim 6, wherein the electric potential cycles from a negative voltage to a positive voltage and back to a negative voltage.

Claim 17 is drawn to the composition of claim 16, wherein the plurality of morphogens comprises fibroblast growth factor, transforming growth factor beta, or both. (Applicant has elected fibroblast growth factor.)

Wolf teaches a method for stimulating cells with an electrical current where the cells are incubated for about 1-2 days (column 20 line 34) and exposed to a waveform current (column 10 example 6). The resulting morphogen composition is collected prior to harvest of cells and shown by additional testing of the cells to contain a plurality of growth factors including fibroblast growth factor (column 18 line 24). Even though the reference does not explicitly teach the collection of the morphogen composition, it is inherently practiced and taught, as this step is required for the cell harvest to occur. The reference also teaches that the time varying current applied to the cells is an alternating current which changes from negative potential to positive potential and back to negative

potential (column 20 lines 1-25). The media that the cells are incubated in is a biocompatible fluid (column 8 example 2).

Claims 11-14 and 46 are rejected under 35 U.S.C. 102(e) as being anticipated by Rueger et al (US 6,495,513 B1).

Claims 11 and 12 are drawn to the composition as described above.

Claim 13 is drawn to the composition of claim 12, wherein the fluid is a buffer.

Claim 14 is drawn to the composition of claim 12, wherein the fluid is a gel.

Claim 46 is drawn to a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a morphogen composition of claim 11.

These claims are product-by-process claims and even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.

Rueger teaches a morphogen composition that contains phosphate-buffered saline in a gel in a silicone tube carrier (column 37 line 20-27). The specific addition of a pharmaceutically acceptable carrier is taught as well (column 27 line 19-25).

Rueger explicitly teaches all the limitations of Applicant's claimed invention.

Claims 1-5, 10-12, 15-18 and 46 are rejected under 35 U.S.C. 102(e) as being anticipated by Stringer (US 2005/0053596 A1).

Claims 1-5 are drawn to the method as described above.

Claim 10 is drawn to the method of claim 1, further comprising removing cells from the extracellular matrix to form a cell-free extracellular matrix.

Claims 11, 12,16,17 and 46 are drawn to the composition as described above.

Claim 15 is drawn to the composition in lyophilized form.

Claim 18 is drawn to the composition of claim 11, wherein the extracellular matrix is cell-free.

Stringer teaches a morphogen composition and a method of forming it wherein the steps include culturing cells, harvesting the extracellular material produced by the cells (which removes the cells), isolating and purifying the material, and lyophilizing the material (claim 16). The extracellular material is taught to contain a highly complex mix of cytokines, growth factors, matrix and other proteins (p.5 para 98). The addition of a physiologically acceptable carrier is taught as well (claim 17).

Stringer explicitly teaches all the limitations of Applicant's claimed invention.

Claims 1-6, 8, 9, 11, 12, 19, 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Wong et al (US 5,843,741).

Claims 1-6, 8 and 9 are drawn to the method as described above.

Claims 11, 12, and 19 are drawn to the composition as described above.

Claim 20 is drawn to the composition of claim 19 wherein the electric potential is a negative potential.

Wong teaches a method for altering the differentiation of anchorage dependent cells on an electrically conducting polymer by applying a voltage range between –0.25 and 0.1 V to a cell culture (column 13 line 31). A specific example wherein the electric potential is a negative potential is also taught (column 15 line 53). The morphogen composition was collected each time a culture was washed or fed with new media (column 19 line 60) which is also a biocompatible liquid. While the reference is silent to the presence of exactly which morphogens are in the composition, they are inherently the same as Applicant's (a plurality of morphogens) since the reference is carrying out the same method as claimed by Applicant.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura Schuberg whose telephone number is 571-272-3347. The examiner can normally be reached on Mon-Fri 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Laura Schuberg

SANDRA E. SAUCIER
PRIMARY EXAMINER